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Date Due 2-29-2000 Serial No. 08/905,293

Date Mailed 2-28-2000 Docket No. ~~DN01146A~~ DN01146A

Attorney Chas Klein

OIPE JC67 MAY 08 2000 PATENT & TRADEMARK OFFICE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Dale E. Yelton et al.	Art Unit:	1641
Serial No.:	08/905,293		
Filing Date:	August 1, 1997	Examiner:	S. Devi
Title:	Method for Inhibiting Immunoglobulin-Induced Toxicity Resulting From the Use of Immunoglobulins in Therapy and In Vivo Diagnosis	Atty. Docket:	ON0146A

Princeton, New Jersey 08543-4000
February 28, 2000*

AMENDMENT AND RESPONSE

Assistant Commissioner for Patents:

Sir:

This paper is filed in response to the final Office Action dated August 31, 1999. A request for a 3 month extension of time in which to file a response, and the appropriate fee, is enclosed herewith.

Claims 1 to 22 and 28 to 31 are currently pending. Applicants acknowledge the Examiner's withdrawal of rejections based on 35 U.S.C. 112.

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Assistant Commissioner For Patents, Washington, D. C. 20231 on February 28, 2000.

Lisa B. Swidra — 2/28/2000

Lisa B. Swidra — Date

35 US.C. 102(b)

The Examiner has maintained the rejection of Claims 1, 2, 5 and 7 to 10 under 35 U.S.C. 102(b) as being anticipated by Morgan (WO 94/29351). Applicants disagree.

A claim is anticipated only if each and every element, as set forth in the claim, is found in a single prior art reference. Verdegaal Bros. V. Union Oil Co. of California, 2 USPQ 2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the...claim." Richardson v. Suzuki Motor Co., 9 USPQ 2d 1913, 1920 (Fed. Cir. 1989).

The rejected claims cover a method for inhibiting toxicity resulting from immunoglobulin immunotherapy by administering an immunoglobulin molecule that has been modified by "structurally altering multiple toxicity associated domains" in the immunoglobulin molecule. The specification, at page 8, defines "multiple toxicity associated domains" as:

> more than one discrete toxicity associated domain. As there appear to be at least two toxicity associated domains in the immunoglobulin molecule, one roughly localized to amino acids 231-238 and another roughly localized to amino acids 310-331, an example of the structural alteration of multiple toxicity associated domains comprises the insertion, substitution or deletion of amino acid residues in both of these domains. This definition excludes structural alterations targeting a single toxicity associated domain.

It is clear from the claim that the immunoglobulin molecule must be modified in more than one toxicity associated domain. The Morgan reference does not disclose modifying an immunoglobulin molecule in more than one domain. Morgan discloses mutations in only one domain, namely amino acids 231-239 (Morgan, page 6).

The Examiner argues that "alteration of the whole regions 233, 234, 235 and 236 (i.e., multiple regions) by exchanging with the sequence found in IgG2 abolished multiple functional properties..." (Office Action, page 6). This, however, is nothing more than a poor attempt to argue each individual amino acid is a separate "domain". Morgan discloses amino acids 231-239 as one domain, and completely fails to disclose modification of any other domain.

Because the claim limitation of requiring modification of multiple (i.e., more than one) toxicity domains is missing from the Morgan reference, as well as lacking any teaching or immunoglobulin induced toxicity resulting from immunoglobulin therapy, Applicants submit that it is legally impossible for Morgan to anticipate the claimed invention. The Examiner is respectfully requested to withdraw the rejection of Claims 1, 2, 5 and 7-10 under 35 U.S.C. 102(b).

35 U.S.C. 103(a)

The Examiner has rejected Claims 3, 4, 6 and 11-12 under 35 U.S.C. 103(a) as being unpatentable over Morgan (WO 94/29351), and in view of Yelton (U.S. Patent 5,792,456) or Muroi, taken with Gillies. Applicants disagree.

In order to render the instant claims obvious, in view of the cited references, there must be some suggestion, found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, for combining the references. In re Jones, 21 USPQ 2d 1941, 1943-44 (Fed. Cir. 1992). Conspicuously missing from the record in this case is any evidence, other than the Examiner's speculation, that one skilled in the art would have been motivated to combine the cited references, and that such

combination would successfully yield Applicants' invention. See Jones, at 1944.

As discussed above, and in previous responses, Morgan is lacking in any suggestion of several claim limitations, including the use of immunoglobulins that have been altered in multiple toxicity associated domains. The deficiencies of Morgan are not remedied by the teachings of Yelton, Muroi and/or Gillies.

While Yelton et al. provides teachings about mutant BR96 as a composition of matter and its use in some contexts, this reference does not disclose Applicants' claimed methods for inhibiting immunoglobulin-induced toxicity. In particular, while Yelton notes that functional equivalents of mutant BR96 antibody which do not include the Fc region do not exhibit ADCC or CDC properties, a combination of this reference with Morgan does not teach that antibodies having alterations in multiple toxicity associated domains can be used in methods for inhibiting immunoglobulin-induced toxicity. Moreover, because the biological significance of the amino acid residues in the C-terminal domain is disparaged in Morgan et al., one skilled in the art would be disinclined to combine these references in the manner suggested by the Examiner. In particular, even if one was to try to combine such disparate references, the resulting combination would not successfully generate the claimed invention. Therefore, the claimed invention cannot be obvious in light of these references. For this reason, Applicants respectfully request the withdrawal of this rejection.

Muroi et al. simply disclose antibodies that recognize and bind to Le^x. This reference does not overcome the deficiencies in the other references cited by the Examiner and a combination of these references does not teach or suggest that antibodies having alterations in multiple toxicity associated

domains can be used in methods for inhibiting immunoglobuoin-induced toxicity. For this reason, Applicants respectfully request the withdrawal of this rejection.

Finally, while Gilles et al. provides a method for mutating the constant region of a human gamma chain and note that these mutants exhibit little ADCC or CDC activity, a combination of this reference with Morgan does not teach that antibodies having alterations in multiple toxicity associated domains can be used in methods for inhibiting immunoglobulin-induced toxicity. Moreover, because the biological significance of the amino acid residues in the C-terminal domain is disparaged in Morgan et al., one skilled in the art would be disinclined to combine these references in the manner suggested by the Examiner. In addition, even if one was to try to combine such disparate references, the resulting combination would not successfully generate the claimed invention. Therefore, the claimed invention cannot be obvious in light of these references. For this reason, Applicants respectfully request the withdrawal of this rejection.

Because the referenced cited by the Examiner fail to contain some suggestion, either explicit or implicit, of the combination proposed by the Examiner, the rejection must fall. In re Bell, 26 USPQ 2d 1529, 1531 (Fed. Cir. 1993) (Obviousness "cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination.")

Moreover, lacking from each and every reference, taken alone or in combination, is the necessary claim element of alterations to multiple toxicity associated domains of an immunoglobulin molecule. It is impossible for the claims to be rendered obvious when all of the claimed elements are not present

in the references. Since the references cited by the Examiner fail to teach or suggest the limitations of the pending claims, the rejection must fall. Motorola Inc. v. Interdigital Technology Corp., 43 USPQ2d 1481, 1490 (Fed. Cir. 1997) (Federal Circuit reversed an obviousness determination because "no combination of prior art references for obviousness describes the four particular functions recited in the claim...").

The Examiner also rejected Claims 28 to 31 under 35 U.S.C. 103(a) as being obvious over Morgan in view of Yelton. Applicants disagree.

Applicants point out that Morgan does not teach or suggest methods for inhibiting immunoglobulin induced toxicity by using antibodies having modifications in multiple toxicity associated domains, as described in detail above. Yelton fails to remedy Morgan's insufficient disclosure. Because there is no suggestion found in these references to combine and successfully achieve the claimed invention, and claim elements are missing from the cited references, the rejection must be withdrawn.

Conclusion

In light of the above, Applicants respectfully submit that the pending claims are neither anticipated nor made obvious by the cited art, and request that the application be allowed. The Examiner is invited to call Applicants' attorney to expedite allowance of the application.

Respectfully Submitted,

Date: February 28, 2000

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